NavMed 369 RESTRICTED

NAVY DEPARTMENT

BUMED NEWS LETTER

a digest of timely information

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Vol. 5 Friday, June 22, 1945 No. 13

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Treatment of Motion Sickness - Ineffectiveness of Benzedrine and Ephedrine: Since commercial preparations containing benzedrine (amphetamine) sulfate and ephedrine sulfate are on the market as correctives for motion sickness, it is pertinent to point out that neither of these drugs, used singly or in combination, is effective in the prevention or treatment of seasickness or airsickness. In one laboratory investigation, for example, it was found

that benzedrine sulfate in oral doses of 10 mg., given two hours before swinging, produced no significant change in the incidence of swing sickness. Other trials of benzedrine and ephedrine, both in this country and elsewhere, have proved uniformly disappointing, and there is no reason to believe that either of these drugs is of value in the prophylactic or therapeutic management of motion sickness in naval personnel. Their use for this purpose is, therefore, not recommended.

Research on motion sickness has indicated that hyoscine in a dose of 0.65 mg., administered about one hour before the effect is desired, is effective as a preventive in a certain percentage of cases. This dose may be repeated after eight hours, but more than this should not be used without medical supervision. Other motion sickness remedies developed by the Army and by the Royal Canadian Navy seem to be about as effective as hyoscine alone.

Remedies for motion sickness are not recommended for routine use by naval personnel. It is clear that individuals unable to overcome susceptibility to motion sickness through habituation cannot be maintained for long periods in a state of operational efficiency by dependence on drugs, and that they must ultimately be removed from duties likely to produce the condition. Since possible undesirable side effects of such drugs are not yet sufficiently well understood, this is particularly applicable to naval aviators for whom motion sickness preventives or remedies are not considered suitable, especially under combat conditions.

Within the naval service, it is important to recognize those individuals whose operational efficiency is impaired by motion sickness and to exclude them from certain types of duties. Correct initial indoctrination and training are of great importance in preventing the establishment of a sickness pattern of response to unusual motions. As an aid to habituation during such periods of indoctrination, recourse may be had to hyoscine administered under careful medical supervision. At sea, as well as in the air, personnel must learn to disregard, to some extent at any rate, the symptoms of sea- or airsickness. (Res. Div., BuMed - E. C. Hoff)

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The Treatment of Progressive Bacterial Synergistic Gangrene with Penicillin: Progressive bacterial synergistic gangrene is a serious infection caused by the synergistic action of a microaerophilic, nonhemolytic streptococcus and a Staphylococcus aureus. This infection is characterized by a slowly spreading, superficial ulceration of the skin. The advancing margin is a zone of erythema in which the microaerophilic, nonhemolytic streptococcus may be found in pure culture. Within this zone, there is a raised, purple, necrobiotic zone which is usually extremely painful and tender to touch and on

its inner margin, closely attached to it, there is a zone of gangrenous skin which has the appearance of suede leather. The inner margin of the gangrenous zone is slightly undermined and gradually liquefies as the process advances. Within the necrotic zone there is a gradually enlarging, granulating surface where residual islands of epithelium frequently start a reparative process.

The lesion most frequently develops either on the chest wall following the drainage of a putrid empyema or on the abdominal wall following the drainage of an intraperitoneal infection. Many other organisms may contaminate these ulcers and even become important as secondary invaders.

Heretofore, the only cure for this condition was wide excision followed by the application of antibacterial agents designed to prevent the activity of these organisms and recurrence of the infection. The essential organisms are susceptible to penicillin and three cases have been reported in two of which a prompt cure was effected without the necessity for surgery. In the third case, there was improvement, but the beneficial effect of penicillin was nullified by the presence and activity of E. coli and Ps. aeruginosa (B. pyocyaneus). Penicillin in large doses should be used early in the treatment of this infection and may be expected to effect a cure unless the action of the drug is interfered with locally by secondary contaminants, which are capable of producing penicillinase. (OEMcmr-80 - Meleney, Friedman and Harvey - Abstract of Ms. for Publication - March 5, '45)

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Pain in Wounded Men: Severe wounds are often associated with surprisingly little pain. In order to get factual information on the incidence of pain, two hundred and twenty-five recently and seriously wounded men were considered in five groups: compound fractures of long bones, extensive peripheral soft tissue wounds, penetrating wounds of the thorax, penetrating wounds of the abdomen, and penetrating wounds of the cerebrum. None of these men was in shock at the time of questioning. As nearly as possible consecutive cases were considered. Ten of these had to be eliminated from consideration here because they were not clear mentally or were unconscious. Nine of these ten had penetrating head wounds. If the group of patients with head wounds is entirely disregarded, only one patient out of the remaining two hundred and one severely wounded was not alert and clear mentally.

Patients with penetrating wounds of the abdomen had by far the most pain, possibly resulting from the spilling of blood and intestinal contents into the peritoneal cavity. Of all the patients considered, only one-quarter, on being directly questioned shortly after entry in a forward hospital, said that their pain was enough to cause them to want medication for relief of pain.

Three-quarters of them did not need such relief. This was the case notwithstanding the fact that the only morphine given had been administered many hours before. The difference between those who wanted pain-relief therapy and those who did not cannot be explained by differences in dosage or timing of the morphine administered. It is believed that morphine is too often administered by rote and not according to the patient's need. It would appear that morphine is frequently used in the belief that severe wounds are inevitably associated with severe pain, which is clearly not the case.

In some cases, it was observed that the excitement and hyperactivity occasionally encountered in the wounded had its origin not in pain but in cerebral anoxia, and more commonly in mental distress. The use of a small dose of a barbiturate provided great relief in the latter type of case. Small doses of barbiturates or narcotics will accomplish what large doses often fail to do. Barbiturate sedation is of great value in the treatment of the wounded man. He often needs the type of mental depression produced by barbiturates in small dosage as much as he needs the pain depression produced by morphine. The man in shock complains far less frequently of wound pain than he does of the great distress produced by thirst. (Med. Bull. Mediterranean Theater of Operations, March '45 - Beecher)

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Ineffectiveness of Mapharsen as a Cure for Malaria: Much has been written concerning the treatment of malaria with arsenical compounds, and an examination of health records reveals rather widespread use of arsenical compounds which are intravenously administered in the treatment of chronic malaria. A review of the literature leaves no doubt that the preparations used have some therapeutic value, although it has not been established that any cures have been effected by this treatment. Because of the tenacity of some vivax malaria infections acquired in the South Pacific area, it was felt justifiable to determine the actual value of mapharsen as a curative drug for malaria by intensive intravenous administration.

Sixteen patients were selected, all of whom had experienced almost monthly recurrences of clinical vivax malaria for a period of over two years. These patients were started on intravenous mapharsen and were given, in addition, a total of 3.2 Gm. of atabrine for a week. The dosage of mapharsen was 0.06 Gm. three times weekly until a total of 20 mg. per kilo of body weight was given. The average number of doses was 26, and the duration of treatment was from 7 to 10 weeks. During the treatment period parasitemia disappeared; there were no relapses. In general, patients showed subjective improvement and gained in weight.

All of the patients have been observed for one month since completion of treatment and some patients for two months. During this period 6 of the patients

(37 per cent) have already relapsed. This rate of relapse within 2 months after this intensive course of treatment affords conclusive evidence that mapharsen will not cure this form of malaria acquired in the South Pacific.

Since other drugs satisfactorily curb the acute attacks of malaria, it is recommended that intravenously administered mapharsen, a potentially dangerous drug, not be employed in the treatment of relapsing, vivax malaria. (Marine Barracks, Klamath Falls, Ore. - L. T. Coggeshall)

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Comments on X-Ray Therapy in the Navy: In the Bumed News Letter of December 28, 1944, there appeared a note advising caution in the use of X-ray therapy for dermatological conditions. This warning should be amplified and emphasized.

X-ray and radium rays produce certain effects in living tissues, probably by causing ionization in the tissue cells. In certain inflammatory conditions the effect of the rays, in proper dosage, is beneficial. As a general rule, the more acute the inflammation the smaller should be the dose of rays; also, when a large area is treated, the dosage must be less than that used for a small area. The voltage and filtration employed vary according to the depth and thickness of the lesion to be treated.

Large doses of X-rays, or radium rays, cause destruction of tissue cells, and such large doses are used in the treatment of neoplasms. Even a small dose will cause some tissue change; the effect is cumulative, and repeated small doses may result in late skin or tissue changes which may be disfiguring or disabling. A large dose, given at one time, or in repeated fractions in a short period of time, may cause a marked reaction, followed by late changes. Unfortunately, there is no immediate, visible result to warn of the impending damage. Repeated small doses of X-rays or radium, or repeated series of treatments, may cause late telangiectasis, skin atrophy, or ulceration and necrosis, even though the individual treatments or series of treatments may have caused little visible reaction. The therapist must know and observe the limits of safety in dosage.

In some places X-ray therapy is used too freely, particularly for skin diseases. MacKee (X-rays and Radium in the Treatment of Diseases of the Skin, 3rd Edition) lists about ninety skin diseases "in which X-rays and radium have been found useful". However, it is not good practice to use X-ray therapy as a routine in all of these conditions, and in only a few, probably less than a dozen, is X-ray therapy the best method of treatment. Whenever possible, skin diseases should be treated by a dermatologist. When X-ray therapy

is used, there should be close cooperation between the dermatologist,or other clinician,and the roentgenologist in order that proper cases for X-ray therapy may be selected and the use of incompatible drugs or local applications during X-ray therapy may be avoided.

When X-ray therapy is used, it should be given by a qualified roentgen therapist, using accurately calibrated equipment. A complete record of all treatments should be entered in the patient's health record, including the factors of voltage, filtration, skin target distance, size of fields, areas treated, and the dosage in r units. Such entries should be kept in the current record as long as the individual is in the Service. No additional roentgen or radium therapy should be given to any area without consulting the record of previous treatments.

In the Navy, chronic and recurrent skin lesions should not be treated with X-rays. These conditions require a series of treatments over a period of several weeks or months, and only in a small percentage of cases are the results any better than with other methods of treatment. It is not a good plan to have X-ray therapy given at irregular intervals by several or many therapists, no one of whom will have the opportunity of continuous observation of the case. Such therapy is not likely to produce good results, and is most likely to lead to undesirable late skin changes. In any case, when the patient will not be available for the complete course of treatment and for a proper period of observation, it is wise to refuse X-ray therapy.

The two most frequent dermatological entities for which X-ray therapy is requested are acne vulgaris and dermatophytosis. Under ideal peacetime conditions, the value of X-ray therapy in such cases is debatable; under wartime conditions in the Navy, such cases should not be considered for X-ray therapy.

In the treatment of neoplasms or any condition requiring destructive dosage, the mode of therapy should be selected to fit the individual case. Consultation with surgeons, internists and other specialists should be utilized to select the best method of treatment. Whether surgery, electrotherapy, the use of X-ray or radium, or a combination of two or more of these agents be used, it is of vital importance that the first treatment be adequate. After inadequate treatment by any method, proper treatment is more difficult. This is more evident following inadequate irradiation than after any other procedure. When tissues have been subjected to relatively large doses of X-rays, there is likely to be delayed healing or sloughing after surgery. If adequate dosage of X-rays or radium is given to these damaged tissues there will probably be sloughing with persistent ulceration or late radiation necrosis.

There is seldom, if ever, a need for immediate X-ray therapy in skin diseases or superficial cancers. If the equipment at hand is not adequate and is not

accurately calibrated, or if the roentgenologist has not had training and experience in roentgen therapy, treatment should be deferred until the patient can be given the benefit of proper therapy. (USNH, Portsmouth. Va. - W. H. Whitmore)

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The Cornell Service Index: Weider et al have devised the Cornell Service Index (Form S) as a simple means of obtaining and evaluating psychiatric data of significance from men who have been in military service for at least a month. The test is self-administered and may be given to many subjects simultaneously. It can be completed by the subjects in ten minutes and can be scored within one minute.

Warner and Gallico have found that the responses obtained by this test distinguish with a high degree of accuracy patients without apparent personality disturbances from those who present psychiatric complaints of significant degree. The form does not effect a very clear separation between mild and severe personality disturbances, although it is of some help in this differentiation. It is a useful research instrument in obtaining groups of patients for comparison according to the presence or absence of psychiatric determinants.

The use of this form reveals a small number of persons with histories replete with psychoneurotic symptoms who are not thereby prevented from performing their duty adequately. This apparent discrepancy may be partially explained by the factor of motivation toward the service. The results obtained on the form correlate closely with the histories obtained on interview. It is, therefore, of use in obtaining histories rapidly in the psychiatric service or at a psychiatric consultation.

The form does not reveal adequately the histories of subjects who are lacking in awareness of their difficulties. It does not uncover many cases of conversion hysteria, and it does not concern itself with sexual disturbances. It does apply adequately to the great majority of patients who come to the attention of the military psychiatrist, and it should prove to be of considerable use in the evaluation of psychiatric disturbances in members of the Armed Service. (War Med., April '45)

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Poliomyelitis Virus in Contaminated Food: Much evidence has accumulated during recent years which suggests that the alimentary tract (mouth and pharynx to colon) may be a portal of entry for the virus of poliomyelitis in humans. The virus has been demonstrated repeatedly in human

stools, in sewage and in flies, but there has been no direct evidence that contact with infected fecal material, with sewage or with flies bears any relationship to the infection of humans by this virus.

Ward et al have produced subclinical infections or carrier states of poliomyelitis in chimpanzees by feeding them with food which had been exposed to flies in the homes of patients with the disease during an epidemic. The virus of poliomyelitis was demonstrated in the stools of these chimpanzees by the intracerebral inoculation into rhesus monkeys of suitable preparations of the stools. (Science, May 11, '45)

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General Anesthesia in Shock: Crooke and his associates have indicated that operations on seriously shocked patients are associated with an extremely high mortality. This may be due to further loss of blood entailed during the operation, to the stimulus of the operative manipulations, or to the anesthesia. It has become apparent that the most important single factor has been the anesthesia, and an examination was therefore made of the effects of different anesthetic agents on the cardiovascular systems of 26 patients with normal plasma volumes, of whom 19 underwent major operations.

The anesthetics used were nitrous oxide, oxygen and ether, cyclopropane and oxygen, sodium pentothal and spinal analgesics. In all cases the pulse, respiratory rate and blood pressure were recorded at about three-minute intervals. Determinations of plasma volume were made, and the dye concentration curves were followed at about thirty-minute intervals until the end of the operation. The hemoglobin was also determined at the same intervals. Electrocardiographic records were made of nine of the patients.

No significant changes were found, except that great alterations in blood pressure occurred. It was concluded that anesthetic agents affect blood pressure mainly through the vasomotor system. Cyclopropane and oxygen tended to raise the blood pressure; nitrous oxide, oxygen and ether had variable effects on it; sodium pentothal and spinal analgesics depressed it. In a patient whose plasma volume was reduced by trauma there was a greater tendency for these anesthetics to depress blood pressure. In this series it was concluded that a combination of cyclopropane and oxygen was the best anesthetic and nitrous oxide with adequate oxygen and a minimal amount of ether was the next best anesthetic. (Brit. M. J., Nov. 25, '44)

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Circulatory Effects of Human Albumin Solutions in Patients with Shock: Concentrated human albumin without additional crystalloid solution was injected

into twenty-two surgical patients with hypotension and oligemia. Circulatory measurements were made before, 20 minutes after and, in eleven cases, two and one-half hours after the injection. The results indicate that the injected albumin produced a decrease in hematocrit (average from 39 to 33) and an increase in plasma volume (average 11.4 cc. per Gm. of albumin injected).

The mean arterial blood pressure, although it rose approximately 17 mm. Hg., did not return to the accepted normal level. This confirms previous observations that following rapid hemodilution with a decrease in the apparent blood viscosity, changes in arterial blood pressure are not an adequate index of the restoration of the circulation. In other words, in these cases, the circulation was satisfactorily restored although mean arterial blood pressures were still subnormal. (OEMcmr-107 - Cournand, Columbia Univ. - CMR Bulletin #38)

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Renal Function of Dogs Given Oxyhemoglobin or Methemoglobin Solutions: After withdrawal of 50 cc. of blood per kilo from dogs, anuria resulted for about 12 hours unless the withdrawn blood was replaced by other fluid. Replacement of the blood by an equal volume of sterile plasma, 7.6 per cent oxyhemoglobin, or 7.6 per cent methemoglobin solution, at once restored the flow of urine.

The urea clearance of dogs infused with plasma or oxyhemoglobin solution returned to preoperative levels the day following infusion, except in the case of one dog infused with oxyhemoglobin. This animal showed an unexplained transitory fall in urea clearance on the third postoperative day. In dogs infused with methemoglobin solution, the urea clearances remained depressed to about one-third normal for three days, returning to normal during the next three days. Renal function then remained normal.

The half-life of either injected oxyhemoglobin or methemoglobin in the circulating plasma was about eight hours. All pigment disappeared in 72 hours. During circulation in the plasma little infused oxyhemoglobin changed to methemoglobin, but a large part of infused methemoglobin changed to active hemoglobin. From 30 to 40 per cent of the injected pigment, infused as either oxyhemoglobin or methemoglobin, was excreted in the urine. (OEMcmr-67 - Van Slyke, Rockefeller Inst. for Med. Res. - CMR Bulletin #38)

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Significance of Blood Amino Acid Concentration: Surprisingly little work has been done by recent methods upon the physiologic variants of the amino acids of the blood. Nevertheless, variations in the concentrations of amino acids in

blood, as determined by these methods, are being interpreted without adequate physiological controls. It has been assumed that the concentration of amino acids in the serum might serve as an index of the metabolism of protein in the body. In the course of studies of the nitrogen metabolism in various diseases, data have been accumulated that cast some doubt upon this concept.

In a variety of patients with infectious diseases, injuries and surgical operations, the blood amino acid concentration (by the ninhydrin method of Hamilton and Van Slyke) showed little correlation with the total turnover of protein (the total nitrogen intake or nitrogen output, whichever was larger, during the preceding 24 hours).

It is noteworthy that, despite the fact that the turnover of protein usually exceeded 100 Gm. per day, in only three instances did the concentrations of amino acids exceed the normal limits (in each instance by a negligible amount), while in eleven instances the amino acids fell below the normal limits. One of the patients with the highest turnover of protein, more than 200 Gm., had the lowest amino acid concentration in the series. (OEMcmr-420 - Man and Waife, Yale Univ. - CMR Bulletin #37)

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The Diagnosis and Disposition of Cases of Minimal Pulmonary Tuberculosis: The mass screening of Naval and Marine Corps personnel by photofluorography has resulted in a significant increase in the percentage of cases discovered of minimal pulmonary tuberculosis. All cases in which suspicious shadows are present in the photofluorogram are subjected to clinical study for diagnosis and disposition. The full responsibility for the prognosis of such a case rests on the judgement of the medical officer in establishing the diagnosis and in recommending proper disposition of the case. Account must be taken of the activity of the lesion and the possible effect of continued naval service on it. Cases are on record in which lesions of minimal tuberculosis were missed on the photofluorogram or were considered to be of no clinical significance by the cognizant medical officer, and which progressed under service conditions to a moderately advanced or far advanced stage before again coming under medical care.

The physician in charge of the photofluorographic unit is charged with the responsibility of the screening process and of recommending for further clinical study all cases in which a pathological lesion is suspected. Listed below are the causes for rejection for original entry into the Service according to the directive, BUMED-Y-DFS, P3-3/P3-1(054-40), dated 4 Jan 1945:

(a) Any evidence of reinfection (adult) type tuberculosis, active or inactive, other than slight thickening of the apical pleura or thin solitary fibroid strands.

(b) Evidence of active primary (childhood) type tuberculosis.

(c) Extensive multiple calcification in the lung parenchyma, or massive calcification in the hilus, or any calcification of questionable stability.

(d) Evidence of fibrous or sero-fibrinous pleuritis, except moderate diaphragmatic adhesions with or without blunting or obliteration of the costophrenic sinus.

(e) Other disqualifying defects demonstrable by a roentgen examination of the chest (See paragraph 1477, Manual of the Medical Department).

Under this same directive, these conditions are, in addition, causes for further clinical study of personnel who have been previously accepted for naval service. Once the individual with a suspected pathological lesion has been hospitalized, the full responsibility for the clinical investigation and diagnosis rests upon the medical officer of the hospital.

When a suspicious roentgenological shadow is demonstrated, a diagnosis must be established. Ordinarily this can be accomplished only after a period of weeks of careful investigation. A detailed history and a thorough physical examination are necessary. Although pulmonary tuberculosis in its early stages is not often associated with appreciable symptoms or physical signs, observation of the patient's course will assist materially in differentiating the suspected lesion from pneumonia, bronchiectasis, lung abscess, neoplasm, chronic upper respiratory infection, pulmonary fungus infection and the various pulmonary fibroses. A tuberculin test should be done, a procedure of particular value for ruling out tuberculosis when a negative result is obtained.

Repeated examinations of sputa for tubercle bacilli should be made on specimens which have been concentrated. The proper collection of the specimen is as important as a painstaking laboratory examination. Saliva is too often sent to the laboratory as a result of lack of instruction of patients. When repeated specimens have been found negative, cultures and inoculation of animals should be done. When all other methods have failed, and in patients who have little sputum, attempts should be made to demonstrate tubercle bacilli by smear, culture and inoculation into animals of concentrated stomach washings.

In order to determine whether or not a lesion is active, it is necessary to obtain a series of X-ray films over a period of weeks. The patient's temperature should also be followed carefully and laboratory procedures must include, in addition to careful sputum studies, sedimentation rate of erythrocytes and white and differential blood cell counts.

Extreme caution should be exercised in returning a man to duty with the established diagnosis of "reinfection tuberculosis, minimal, arrested". If his disease is not actually arrested, the one opportunity of affecting a cure may thus be lost, and the prognosis of his disease completely altered. The 1940 edition of "Diagnostic Standards", published by the National Tuberculosis Association, classifies pulmonary tuberculosis as arrested only after a period of six months' observation during which time the X-ray lesions have remained stationary, constitutional symptoms have been absent, and concentrated sputa, examined at monthly intervals, have been negative for tubercle bacilli. (Prev. Med. Div., BuMed - T. J. Carter)

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Prophylaxis of Wound Infection: Peterson has investigated the prophylaxis of wound infection in dogs. Both clean and contaminated wounds were studied. There is no doubt as to the efficacy of the various soaps as germicidal agents. However, in these experiments, when the soaps were placed in actual contact with uncontaminated fresh wounds, they produced a definite but slight irritation. This was noted only on microscopic examination; gross examination revealed no difference between control wounds and wounds into which soap had been placed. However, in wounds which were contaminated by placing a given amount of a culture of Staphylococcus aureus within their depths and then were exposed to soap, there was a definite increase in signs of infection over those found in the control wounds not exposed to soap; "green" soap was found more irritating than "white" soap.

The harmful effect of mechanical washing of the wounds is in direct proportion to the coarseness of the material used. These experiments indicated that of the various methods studied the cleansing of contaminated wounds by a gentle irrigation with isotonic solution of sodium chloride is the most effective prophylaxis of wound infection. Contaminated wounds treated by this gentle irrigation healed with less evidence of infection than did control contaminated wounds subjected to no treatment other than closure. Best results in cleansing these small wounds were obtained by irrigating them with 1,000 cc. of saline solution with no scrubbing, utilizing the force of the stream as the washing mechanism. (Arch. Surg., April '45)

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Effects of Small Molecule Proteins When Injected Parenterally: In the preparation of blood substitutes, conditions may arise in which a partial hydrolysis of protein occurs. The solution may then contain a certain proportion of small molecules. When protein molecules that have a smaller molecular weight than serum albumin (egg white and Bence-Jones' protein) are injected parenterally, they filter through the glomerular membrane and appear in the urine even

when small quantities are given. When bovine albumin (Cohn) is used, however, no increase in protein excretion occurs until large amounts have been injected. With human gamma globulin (Cohn) the largest amounts that can be given produce no such effect.

When egg white, diluted in 0.85 per cent sodium chloride, was injected into rats, there was, after three hours, an increase in hematocrit, in serum urea and in protein in the urine. After six hours the hematocrit was higher (56.2), serum urea was very much elevated (100.4 mg. per cent), and urea clearance was zero. By 17 hours after injection, appreciable amounts of fluid were present in the pleural cavities. Animals sacrificed 48 hours after the injection showed only slight residual effects.

These findings are interpreted to mean that the egg albumin entering the blood stream passed through the capillaries into the subcutaneous tissue spaces where it drew water by means of its colloid osmotic pressure. Because of this, the blood volume became so reduced that renal failure ensued. Recovery occurred when the animals were able to drink enough water to restore their blood volumes. At this point, however, a marked subcutaneous edema developed, as indicated by the accumulation of fluid in the pleural cavities. (OEMcmr-338 - Addis, Stanford Univ. - CMR Bulletin #39)

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Water- and Nitrogen-Sparing Effect of Glucose Ingestion: Experiments have been conducted to determine the extracellular and intracellular water and tissue-sparing effects of glucose in otherwise fasting individuals. Glucose was given in amounts of 50, 100, 200 and 300 Gm. daily over a period of six days. Under conditions of moderate activity, the acetonuria of starvation was found to be very greatly reduced by ingestion of 50 Gm. of glucose per day and almost completely abolished by a dose of 100 Gm. of glucose per day. Approximately the same reduction in urinary nitrogen excretion was accomplished with 100 Gm. of glucose per day as with 300 Gm. per day. On a limited fluid intake the ingestion of more than 100 Gm. of glucose per day is frequently nauseating.

When an intake of 100 Gm. of glucose per day was supplemented by amounts of purified casein, egg protein and wheat germ to replace the 7 Gm. of nitrogen lost in the urine, there resulted but an insignificant improvement in the nitrogen balance. The ingestion of such protein causes an increased demand for the urinary excretion of catabolites, and thus tends to augment the minimum urine volume and minimum water requirement by approximately 200 cc. per day. (OEMcmr-478 - Butler, Mass. Gen. Hosp. - CMR Bulletin #40)

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Effect of Pressure Changes on the Sinuses: The paranasal sinuses when subjected to pressure changes present a situation similar to that of the middle ear. If the openings into the sinuses are normal, air passes into and out of these cavities without any difficulty at any practical rate of ascent or descent, thus assuring adequate equalization of pressure at all times. If the openings of the sinuses are obstructed by swelling of the mucous membrane lining, caused by infections or an allergic condition such as hay fever, or if the openings are covered by redundant tissue on which viscous secretions are present, ready equalization of pressure becomes impossible.

The pressure gradient that is established in pathological conditions during change of altitude produces a pressure differential causing marked pain. Unlike the internal ears, the sinuses are almost equally affected by ascent and descent. If the frontal sinuses are involved, the pain extends over the forehead above the bridge of the nose; if the maxillary sinuses are affected, the pain is on either side of the nose, in the cheekbones. Maxillary sinusitis may produce pain referred to the teeth of the upper jaw, and may thus be mistaken for aerodontalgia. The pain of aerosinusitis, though often of the same type as that caused by ordinary sinusitis at ground level, may be much more severe and fulminating in the event of sudden blockage during rapid change in altitude.

Equalization of pressure to relieve pain in the sinuses is best accomplished by yawning, swallowing or blowing with the nose and mouth closed. Treatment of aerosinusitis should be directed to the obstructed orifices, which usually can be opened by shrinking the nasal mucous membranes with any preparation ordinarily used for this purpose, such as the benzedrine inhaler or a 0.5 per cent solution of neosynephrin hydrochloride. If there is persistent recurrence of aerosinusitis, a search should be made to determine the possible presence of tumors, polyps, scar tissue or other causes of obstruction about the openings of the sinuses in the nose. (Physiol. of Flight, March 15, '45)

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Vitamin C Economy in Human Subjects: Six subjects were saturated with ascorbic acid (400 to 500 mg. daily for from four to six days) and then were placed on a diet lacking in vitamin C but adequate in all other respects. None of the subjects developed scurvy until from five to six months had elapsed, and all appeared to be in good health until two weeks prior to the onset of the disease. Gingivitis appeared only in one case following the advent of perifollicular hemorrhages.

It would appear that the quantity representing an adequate intake of vitamin C should be between the protective minimum (18 to 25 mg. daily) and the

amount required to maintain saturation as evidenced by excretion of vitamin C in the urine (80 to 100 mg. daily). In the absence of clinical evidence, this quantity is largely a matter of conjecture. (Bull. Johns Hopkins Hosp., Nov. '44 - Pijoan and Lozner)

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Tolerance to Amino Acid Mixtures and Casein Digests: Several synthetic mixtures of natural and racemic, crystalline, amino acids suitable for the daily nitrogen requirement have been tested for tolerance in dogs when administered intravenously. Certain mixtures of the ten essential amino acids plus non-essential amino acids, exclusive of glutamic acid, were administered without any resultant obvious sign of disturbance even at rates above 10 mg. of nitrogen per kilogram of body weight per minute for quantities greater than 300 mg. per kilo.

When glutamic acid, natural or racemic, was included in similar mixtures, vomiting reactions frequently occurred when injected at rates above 4 mg. per kilo per minute. Vomiting almost always occurred on the first daily injection containing glutamic acid and usually on any subsequent injection containing more than 100 mg. of glutamic acid per kilo unless given very slowly. Upon the addition of glycine, certain mixtures of the ten essential amino acids were better tolerated.

Two samples of casein digests which were tested usually produced vomiting at injection rates above 2 mg. of nitrogen per kilo per minute, probably because of their content of glutamic acid. No serious reaction has ever occurred as a result of the administration of any mixture of amino acids or casein digest tested. Elimination of minor reactions, such as vomiting, appears possible and is desirable for greater usefulness of these solutions in parenteral feeding. (J. Exper. Med., May 1, '45 - Madden et al)

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Stress as a Cause of Cardiorespiratory Disturbances: Observations were made in apparently healthy individuals of the levels of the pulse rate, blood pressure, circulation and respiration after a fixed amount of exercise and during the usual and unusual emotional states which occur in the course of everyday life. Observations over a ten-month period have revealed the following: On most days the pulse rate, blood pressure, cardiac output (ballistocardiograph), and minute ventilation returned to the resting level within three minutes after exercise. It was noted, however, that on days when fear, anxiety, resentment, and tension were present, the return of these functions to the resting levels was dramatically delayed.

Patients with neurocirculatory asthenia showed these same responses to exercise, and in one the mere recall of the stress-producing situations resulted in increased blood pressure, cardiac output and ventilation. (OEMcmr-508, Wolff, Cornell Univ. - CMR Bulletin #40)

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Fate of Radioactive Carbon Monoxide Administered to Human Subjects: It has been found that a third or more of the carbon monoxide lost from the blood appears to be lost by some route other than the expired air. Recently radioactive CO has been used to study this problem.

Radioactive CO was administered to four normal subjects, and the expired CO_2 was absorbed in soda lime during 15-minute periods thereafter. The maximum conversion to radioactive CO_2 during the periods under study was less than 1 part in 1,000 of the expired CO. Gregersen believes that this is the first really decisive proof that no appreciable oxidation of CO occurs in normal man.

About 150 cc. of CO was administered to three normal subjects, and the whole of their expired air collected for four hours thereafter, the subjects breathing O_2 during this time. From 95 to 96 per cent of the originally administered CO was recovered in the expired air during the four hours of O_2 breathing. These results seem to prove that most of the missing CO in the first hour had combined reversibly with extracirculatory pigments, the extent of such combination being greater than was hitherto suspected.

In the hour after administration of radioactive CO, Geiger counters indicated a much greater concentration of activity over the liver than over other areas, such as over thigh muscles. (OEMcmr-66 - Gregersen, Columbia Univ. - CMR Bulletin #40)

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The Somatic Antigens of Flexner Dysentery Bacilli: The somatic antigens of Shigella paradysenteriae (Flexner) strains have been isolated by a modified acid-extraction procedure which has been successful in the isolation of the "M" protein of Group A, hemolytic streptococci and of the surface antigen of H. pertussis. These dysentery antigens have been studied serologically by immunization and absorption methods, and have been found to be the principal cellular components concerned in agglutination, mouse protection and precipitation of the specific antigen or carbohydrate. Studies of toxicity and antigenicity with these somatic antigens in humans, rabbits and mice show no definite advantage of the isolated fractions over the whole killed bacteria as active immunizing agents. These materials are extremely

antigenic. In one instance, in mice, as little as 0.007 microgram was capable of inducing 50 per cent protection against 100,000 M.L.D. of homologous infecting organisms. (OEMcmr-120, Smolens et al, Univ. of Pa. Ms. for publication. CMR Bulletin #39)

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Improvised Electric Cautery and Ice Pack Bag: A recent report from the 47th Construction Battalion describes methods of improvising in the field two items which may be of interest to personnel of the Medical Department:

Electric Cautery: A lightweight tool for cauterizing may be constructed from materials available in any field electric shop. Holes are drilled to a depth of 1/2 inch in the ends of two pieces of No. 6 bare copper wire, six inches in length, to receive #20 gauge monel heating wire. Holes are drilled in the sides of the copper wire for set screws to secure the heating unit which can be fashioned in any form for the operation required. The two copper wires are taped together, being separated by an insulating material such as mica or fibre, fitted into a light wooden handle, and attached to an extension cord. A direct current of 180 amps - one and one-half volts - may be employed with this apparatus. Six ordinary dry cells in parallel, or a rectifier or D. C. Generator source may suffice.

* *

Ice Pack Bag: An ice pack bag may be constructed from a piece of discarded inner tube which is cut to the desired size and the cut ends vulcanized or patched. A threaded cap, such as may be cut from an old kerosene can, is procured. A small hole is cut into the center of the closed tube, the screw cap body is inserted and secured by vulcanizing or by the use of rubber cement. (Report from the 47th Construction Battalion, Feb. '45)

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Examination of Candidates for Appointment to Officer Rank in Regular Navy: The following extract of BuPers Circular Letter 274-43, dated 27 Dec 1943, is provided for the information of medical officers and to assist them in the proper procedure to be followed in processing examinations of candidates for appointment to officer rank in the regular Navy. Medical officers frequently fail to enclose the certificate indicated in section 2 below:

1. The Secretary of the Navy has recently approved a change in procedure in processing the examinations of all candidates for permanent appointment to commissioned and warrant rank in the regular Navy. Pursuant to the new procedure, the reports of naval examining boards and boards of medical examiners

will not be forwarded to the Office of the Judge Advocate General but to the Chief of Naval Personnel and the Bureau of Medicine and Surgery, respectively.

2. The reports of the various boards of medical examiners will be made only on the appropriate BuMed form and will be signed by each member of the board present and acting. BuMed Form Y is prescribed for all candidates other than Naval Reserve aviators; in the latter cases, Form I. The following certification shall be included in the report: "We hereby certify that the candidate is (not) physically qualified for appointment in the United States Navy as an _____ ." There must in every case be appended to the report a certificate, sworn to by the candidates, as follows:

"I certify that I have informed the board of medical examiners of all bodily or mental ailments which I have suffered and that, to the best of my knowledge and belief, I am at present free from any bodily or mental ailment."

3. A candidate who is found not physically qualified by a board of medical examiners will be so advised and will be informed that, if he so desires, he may undergo the written professional examination. In such a case, the candidate must understand that approval of the findings of the board of medical examiners in the Department will bar him from appointment notwithstanding the fact that he may be found professionally qualified.

--BuPers. L. E. Denfeld

The complete text of Circular Letter 274-43, Pers - 322-KD, P14-2, "Procedure in Processing Examinations of Candidates for Appointment to Officer Rank in Regular Navy", may be found in the Navy Department Semimonthly Bulletin of December 31, 1943. (Med. Records Div., BuMed - C. R. Ball)

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National Institute of Health Research Fellowships: The Public Health Service has announced the creation of National Institute of Health Research Fellowships. These fellowships offer an opportunity for study and research in association with highly trained specialists in the candidate's chosen field at the Institute or some other institution of higher learning. Further information may be obtained from The Director, National Institute of Health, Bethesda 14, Maryland.

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Public Health Foreign Reports:

Disease	Place	Date	Number of Cases
Cholera	India, Calcutta	April 1-14, '45	746 (238 fatal)
Plague	Ecuador	March 3-10, '45	1
	Egypt, Port Said	Feb. 10-24, '45	3
	Madagascar	Feb. 1-10, '45	5
	Morocco (French)	March 21-April 10, '45	27
	Peru	Feb. '45	9 (3 fatal)
Smallpox	British E. Africa, Tanganyika	March 24-31, '45	510 (16 fatal)
		March 10-17, '45	245 (10 fatal)
	Cameroon (French)	March 21-31, '45	195
	Egypt	March 10-17, '45	57
	French Guinea	Feb. 21-April 10, '45	584
	Nicaragua, Managua	Jan. '45	123
	Nigeria	Jan. 27-March 10, '45	553 (66 fatal)
	Sudan (French)	March 21-April 10, '45	243
	Togo (French)	Feb. 21-28, '45	137
	Union of S. Africa	Jan. '45	394 (12 fatal)
	Venezuela	Feb.-March '45	256 (3 fatal)
Typhus Fever	Algeria	March 1-20, '45	132
	Bulgaria	March 24-31, '45	94
	Chile	Jan. 28-Feb. 24, '45	31 (3 fatal)
	Ecuador	March '45	37 (3 fatal)
	Egypt	Feb. 3-10, '45	375 (57 fatal)
		March 10-17, '45	759 (67 fatal)
	Libya, Tripolitania	Jan. '45	7
	Morocco (French)	April 1-10, '45	558
	Turkey	March 3-10, '45	85
		April 7-21, '45	190
	Union of S. Africa	Jan. '45	158 (18 fatal)
	Venezuela	Feb.-March '45	29 (2 fatal)
	Yugoslavia, Croatia	Jan. 1-21, '45	137
Yellow Fever	Ivory Coast, Guiglo	March 13, '45	1 (fatal)
	Peru, Quincemil	April 17, '45	1
	Venezuela, Dantas	Feb. 19, '45	1 (fatal)
	Buen Retiro	April 12, '45	1

(Pub. Health Reps., April 6, May 11 & 18, '45)

To: All Ships and Stations. BuMed-X-BLW:II F34-5

Subj: Personal Decontamination, Liquid Blister Gases. 9 May 1945

Refs: (a) BuMed ltr "Prevention and Decontamination of Mustard Gas and Lewisite Casualties by Use of S-461 Ointment and BAL Ointment, Directions for"; N. D. Bul. Cum. Ed. 1943, 43-1094, p. 473.
(b) BuMed ltr "Personal Decontamination, Liquid Vesicant Gases"; AS&SL Jan-Jun 1944, 44-97, p. 345.

1. GENERAL.

(a) This circular letter is issued as a modification of reference (b). All previous instructions in conflict therewith are canceled.

(b) A specific routine of personal decontamination - that is, self-aid - must be accomplished at once, as prescribed below, if serious eye and skin damage is to be prevented after contamination by liquid blister gas.
This is the individual responsibility of all naval and marine personnel.

(c) However, if battle conditions at the time of exposure compel uninterrupted manning of guns and stations, then personal decontamination shall be accomplished at the earliest possible moment when tactical conditions permit.

DECONTAMINATION OF THE EYES.

(a) Eye shields. The eye shields, supplied to each individual, shall be worn at all times during periods of gas hazard. This prevents contamination of the eye from spray and splashes of liquid blister gases. Periods of hazard would include the handling of vesicant munitions, the use of blister gas in training programs, and at all times when in the open and within range of the enemy aircraft after chemical warfare has been initiated. The eye shields, properly used, constitute the real solution to the problem of eye injuries due to blister gases. If the eye shield is worn, it must be discarded after contamination.

(b) Previous instructions for decontamination. Previous directives contained in references (a) and (b) have stated that irrigation alone should be used as personal decontamination for liquid mustard contamination of the eye. Recent studies have shown that BAL ointment followed by irrigation is superior to irrigation alone. A further advantage of this new personal decontamination procedure is that the individual has to remember only one procedure, since it may be used for all liquid blister gas contamination of the eye. He is therefore not compelled to distinguish between different contaminating agents at a time when this might be impossible.

(c) New procedure.

(1) All contamination of the eyes by any liquid blister gas, whether mustard, nitrogen mustards, lewisite (or other arsenical vesicants) or mixtures thereof, is handled by a new decontamination procedure. This combines the use of BAL ointment, massage and irrigation. Immediately after contamination by any liquid blister gas, BAL ointment is squeezed directly into the lower eyelid. If the eye cannot be opened, as after contamination by lewisite, either alone or in mixtures, the ointment is applied to the eyelids and rubbed well. Sufficient ointment will enter between the lids to relieve pain and spasm to such an extent as to make it possible to open the eye. Ointment shall then be instilled directly into the lower sac. The lids are then closed and massaged for 1 minute. This is followed by irrigation of the eye with water from the canteen or other available uncontaminated source. The head is thrown back, the lids are forced open with the fingers of one hand, while the water is poured into the eye from a container in the other hand. The water shall be poured directly and slowly into the eye for at least 1/2 minute, or until the canteen is empty, but not longer than approximately 2 minutes. If BAL ointment is not immediately available, the eye shall be irrigated immediately with water without waiting to obtain the ointment. The decontamination must be completed before the gas mask is put on in spite of possible exposure to vapor during decontamination.

(2) Liquid mustard alone in the eye causes no immediate pain or discomfort, but when BAL ointment is placed into an eye contaminated with this agent there will be immediate irritation and spasm. This is to be expected and personal decontamination or self-aid should not be stopped because of it. The irritation from the ointment ceases as soon as the irrigation is begun. However, the irrigation should not be stopped as soon as the stinging disappears, but should be continued for 30 seconds to 2 minutes.

(d) Precaution.

(1) BAL ointment placed in an uncontaminated eye is very irritating and causes immediate stinging and spasm which may interfere with the individual's combat ability for a period up to 15 minutes. Therefore, the ointment should be used in the eye only when the individual is fairly certain that his eye has been contaminated by some form of liquid blister gas. The chance of liquid contamination is slight except when in the close vicinity of a shell or bomb burst, or in the path of a direct airplane spray.

(2) The fact that the individual tubes of BAL ointment do not have printed on them directions for use against mustard, nitrogen mustards, and mixtures of these with lewisite is not to be construed as a contraindication to its use against these agents.

(e) Effectiveness of BAL ointment. In contamination of the eye by liquid mustard alone, the initiation of self-aid within the first few seconds is markedly effective and after 2 minutes is of very little value. In the case of contamination of the eye by liquid lewisite or any other arsenical vesicant, BAL ointment is effective for a longer period of time. If it is used within 1 minute after contamination, the eye usually recovers in a few days. When it is used 10 minutes after contamination, the eye requires several weeks to heal and usually suffers permanent damage. BAL ointment has almost no effect after 30 minutes.

3. DECONTAMINATION OF THE SKIN.

(a) Previous instruction. Previous directives contained in references (a) and (b) stipulated that the individual in the field should decontaminate against mustard blister gas by the use of S-461 protective ointment. A new protective ointment designated as Protective Ointment S-330 has since been developed, issues of which were authorized as of 7 December 1944.

(b) Change in standard procedure. An individual at the time of the gas attack, whether by airplane spray, shell or bomb burst, may be unable to ascertain the exact nature of the agent. The hazard of encountering liquid lewisite alone appears small. Liquid lewisite, due to its property and action, is not likely to be used by the enemy other than as a mixture with other blister gases. In view of this situation, the individual shall carry out the following procedure when contaminated with any liquid blister gas unless directed otherwise by local authority:

(1) The free liquid blister gas is blotted from the skin with the absorbent cloth wrapped around each tube of S-330 protective ointment or by using any absorbent material at hand. Discard the used absorbent. Protective Ointment S-330 is then applied freely to the area and thoroughly rubbed into the affected areas with the fingers for about 15 seconds. The excess is immediately removed. In the case of large splashes, the ointment shall be applied and removed once more.

(2) The BAL ointment is then spread on the skin in a thin film, rubbed in with the fingers, allowed to remain at least 5 minutes, and reapplied. BAL ointment sometimes causes temporary stinging and itching urticarial wheals when applied to the skin. These lesions usually last only an hour or so and should not cause alarm. Mild dermatitis is fairly frequent if repeated applications are made to the same skin area. This prevents the use of BAL as a protective film.

(3) The decontaminated skin area should be thoroughly washed with soap and water as soon as practicable following decontamination if such facilities are available.

(4) The individual must familiarize himself with the two ointments. He should know that the large 3-ounce tube contains S-330 protective ointment and the smaller 1-1/2 ounce tube BAL ointment.

(c) Mustard alone. Personal decontamination or self-aid is the removal of liquid mustard at the earliest possible instant by the individual himself. The importance of prompt action cannot be overstressed. Proper skin decontamination from mustard during the first minute is always successful. After 3 minutes on the hot sweaty skin, or 5 minutes on the cool dry skin, no method of decontamination will prevent blistering. Decontamination should be performed, however, no matter how delayed, as long as liquid mustard is still present as it may be of some value. Areas of skin contaminated with liquid blister gas, whether protected by the ointment or unprotected, must be decontaminated as soon as possible. Blot off the excess agent from the skin as described under Change in Standard Procedure, paragraph 3(b), (1) and (3). If the contamination with blister gas is light, no blotting is necessary but generous application of ointment, protective, S-461, or S-330 (preferably the latter), with thorough rubbing will be sufficient. If redness of the skin has appeared before decontamination with protective ointment S-461 or S-330 has been conducted, cleanse the area with soap and water. Protective ointment is irritatng to the reddened skin and shall be used only when liquid mustard is still present and soap and water are not available for thorough washing.

(d) Nitrogen mustards alone. Decontamination and treatment are the same as for mustard. If early decontamination has been neglected, late decontamination should be performed even if erythema is already present and there is no evidence of liquid nitrogen mustard on the skin. The absorption of liquid nitrogen mustards through the skin is slower but more complete than that of mustard. Therefore, for the prevention of systemic toxicity, decontamination should be carried out as late as 2 to 3 hours after exposure, even at the expense of increasing somewhat the severity of the local reaction.

(e) Lewisite alone. If lewisite alone is used, BAL ointment is more effective than protective ointment S-461 or S-330, and should be used, as BAL ointment is effective against all arsenical blister gases on the skin and penetrates through the skin, neutralizing the agent which has been absorbed. Apply BAL ointment as described under Change in Standard Procedure, paragraph 3(b), (2) and (3).

4. Subject ointments are listed in the Medical Department Supply Catalog as follows:

S1-3361	Ointment, BAL; 1/2 oz. tube
S1-3375	Ointment, Protective S-461 and S-330; 3 oz. tube each

One tube of Ointment BAL and one of ointment protective, preferably S-330, shall be provided with each gas mask. Nonmedical activities issuing gas masks shall request these items from the nearest medical supply depot or storehouse. Initial allowance for advance-base personnel will be included in the J15A and B components. It will be noted that ointment BAL is used on the skin and in the eye.

5. In accordance with the policy to replace gradually all issues of Stock No. S1-3375 Ointment Protective, formula S-461, by the formula S-330, all advanced and forward areas, assault troops and combat forces, shall replace S-461 with S-330 as fast as the material becomes available in the areas. Activities in temperate and arctic climates and in rear areas where the possibility of gas attack is remote will replace stocks of S-461 with S-330 when stock is available to meet all requirements. Formula S-461 for which replacement has been made by S-330 should be retained and held as a strategic reserve. --BuMed. Ross T. McIntire.

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ALNAV 100 BuMed 17 May 1945

Subj: Defective Blood Plasma.

Refer Alnav 86. Lot number defective human blood plasma erroneously reported. Correct to read 228395 (two two eight three nine five).
--SecNav. James Forrestal.

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ALNAV 103 BuMed 22 May 1945

Subj: Inoculation Against Cholera.

Naval and civilian personnel traveling under cognizance of Navy Department stationed in and proceeding to or through India shall be inoculated against cholera. --SecNav. James Forrestal.

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To: All Ships and Stations.

BuMed-WM-CM
L8-2/JJ57(042-43)

Subj: Penicillin - Supply, Employment, and Reporting of.

18 May 1945

Refs: (a) Penicillin, Appeals for, to BuMed, L8-2/JJ57(042-43), of 21 Aug 1943.
(b) Letter of Information and Instruction on the Use of Penicillin, L8-2/JJ57(042-43), of 7 Jan 1944.
(c) Medical Stores: Penicillin, L8-2/JJ57(042-43), of 7 Jan 1944; AS&SL Jan-Jun 1944, 44-37, p. 344.
(d) Penicillin Therapy of Gonococcus Infections, Modification of, L8-2/JJ57(042-43), of 23 Feb 1944; AS&SL Jan-Jun 1944, 44-223, p. 359.
(e) Penicillin Therapy of Gonococcus Infections, L8-2/JJ57(042-43), of 19 Aug 1944; AS&SL July-Dec 1944, 44-993, p. 212.
(f) Penicillin Therapy of Early and Latent Syphilis, L8-2/JJ57(042-43), of 15 Sep 1944; AS&SL July-Dec 1944, 44-1119, p. 215.
(g) Penicillin Therapy, Report of Results of, L8-2/JJ57(042-43), of 28 Oct 1944; N. D. Bul. of 28 Feb 1945, 45-193 (enc. (A)).
(h) Penicillin Therapy, Report of Results of, L8-2/JJ57(042-43), of 17 Feb 1945; N. D. Bul. of 28 Feb 1945, 45-193.
(i) Penicillin Therapy of Early and Latent Syphilis, L8-2/JJ57(042-43), of 13 Feb 1945; N. D. Bul. of 15 Feb 1945, 45-148.
(j) "A Guide to Chemotherapy," BuMed News Letter, Vol. 5, No. 6, pp. 8-11, of 16 Mar 1945.

1. References (a), (b), (c), (d), (e), (f), (g), (h) and all other directives pertaining to penicillin, except reference (i), are herewith canceled.

All monthly summaries of the use of penicillin, and the reporting of penicillin therapy in all diseases except syphilis, shall be discontinued. All supply on hand of Medical Supply Catalog item S16-3081, NavMed 140, Penicillin Therapy Report, shall be discarded.

2. (a) Penicillin appears in the Supply Catalog as follows:

Stock No.	Item	Potency Period	Unit
S1-1130	PENICILLIN SODIUM, dry powder, 100,000 Oxford units (equivalent to 60-mg of pure crystalline penicillin).	12 mo.	ampul/vial
S1-1132	PENICILLIN SODIUM, dry powder, 200,000 Oxford units (equivalent to 120-mg of pure crystalline penicillin).	12 mo.	ampul/vial
S1-1131	PENICILLIN CALCIUM, dry powder, 100,000 Oxford units (equivalent to 60-mg of pure crystalline penicillin).	12 mo.	ampul/vial

Stock No.	Item	Potency Period	Unit
S1-1133	PENICILLIN CALCIUM, dry powder, 200,000 Oxford units (equivalent to 120-mg of pure crystalline penicillin).	12 mo.	ampul/vial

Future replenishments to stock for issue to using activities will be made under stock numbers S1-1132 and S1-1133 (200,000 unit vials). Stock on hand under stock numbers S1-1130 and S1-1131 (in 100,000 unit vials) will be issued until present supply is exhausted.

(b) Penicillin is now carried in stock at NMSD, Brooklyn, N. Y., and Oakland, Calif. Quantities requested should not exceed 1 month's requirements except by activities to which shipment may be irregular. Penicillin on hand at any activity, which prospectively cannot be utilized within potency dating, shall be reported as excess, by air mail or dispatch, to BuMed (Material Division, Brooklyn) not less than 2 weeks prior to expiration dating. Such material will be ordered transferred to the nearest activity prepared to use it.

3. The dried powder, when contained in ampules, is quite stable at ordinary room temperature, but high temperatures and prolonged exposure at room temperature cause significant deterioration. To assure maximum potency the ampules should therefore be stored in refrigerators. Though the penicillin expiration date is based upon preservation at ordinary refrigeration temperatures (+4° C.), freezing temperatures will prolong the duration of potency. In liquid form penicillin is unstable. Solutions should be made up preferably just before administration, or at least daily and then kept under refrigeration at about +4° C.

4. The recommended treatment plan for both early and latent syphilis is 40,000 Oxford units of penicillin administered by the intramuscular route every 3 hours day and night, making a total dosage of 2,400,000 units of penicillin given in 60 injections in 7 and 1/2 days. Penicillin is now considered the treatment of choice in early and latent syphilis. When used, it shall be reported as outlined in reference (i). The follow-up studies required in this reference are not being adequately reported to BuMed. All activities are urged to forward these reports as indicated in all cases of penicillin-treated syphilis. Only by thorough follow-up studies can the Bureau determine the success of this treatment plan. It is therefore suggested that, where practicable, personnel who have received the penicillin course of treatment for syphilis not be assigned duty during the ensuing 12 months to activities where facilities for proper follow-up studies do not exist. It is further urged that an individual case be considered a failure only when the Kahn titer fails to drop after 4 months has elapsed since the penicillin routine; or, if it rises after having diminished, in which case it is considered a serological relapse. Clinical relapse, of course, is an indication for retreatment. Retreatment for cases of serological fastness, serological relapse, or clinical relapse, should consist of 4,800,000 Oxford

units administered as 40,000 units intramuscularly every 3 hours day and night for 120 injections in 15 days.

Several treatment plans are being studied by the Subcommittee on Venereal Disease of the National Research Council. The regime herein recommended is part of this long-term program of study, and information accumulated to date indicates that none of the other treatment plans are superior to it. Study of the efficacy of penicillin in CNS syphilis is necessarily in its early stages, and no recommendations can be made at this time.

5. Penicillin is considered the drug of choice in gonococcus infections. Evidence is accumulating that the dosage should be larger than that originally recommended. Fewer failures will be encountered if 20,000 Oxford units of penicillin are given intramuscularly every 2 hours for 7 doses, totalling 140,000 units. The possibility that penicillin therapy of gonococcus infections may mask, abort, or inhibit the development of concomitant cases of early undiagnosed syphilis must be considered. When practicable, therefore, adequate recheck, including serology, of these patients is indicated for at least 3 months.

6. For all other diseases, the dosage and route of administration of penicillin is left to the discretion of individual medical officers. Reference (j) was prepared to assist medical officers when questions arise as to the indications and dosage of penicillin in various diseases and infections.

7. Occasional severe reactions still occur despite progressive improvement in purity of the products now on the market. When severe reactions are encountered, the following data should be forwarded to BuMed:

Diagnosis of case treated; reason for penicillin.
Nature of reaction.
Drugs prescribed concurrently with penicillin therapy.
Has patient received penicillin prior to present administration? If so, give details.
Method and dosage of present administration.
Salt used.
Diluent used.
Manufacturer lot number, and expiration date of penicillin used.
Additional pertinent information.

8. Extensive studies are in progress in search of satisfactory methods to delay the absorption of penicillin. None have been perfected as yet. When safe and reliable methods have been proved, this information will be promptly disseminated. This applies also to the oral administration of penicillin, which has recently received considerable publicity. Although the method appears to have merit, it remains to be proved that an adequate blood level of penicillin can be consistently attained. When administered orally in corn oil, or in water preceded by an alkaline buffer, four to five times the intramuscular dosage is required. The expenditure of this quantity of refined penicillin does not appear justified at the present time. --BuMed. Ross T. McIntire.